

Serial No.: 09/771,355
Filed: January 26, 2001

These amendments are made in adherence with 37 C.F.R. § 1.821-1.825. This amendment is accompanied by a floppy disk containing the above named sequence listing, SEQUENCE ID NUMBERS 1-14, in computer readable form (CRF), and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "Patent-In" provided by the PTO. The information contained in the computer readable disk is identical to that of the paper copy. Additionally the Amendment inserts a paragraph to properly claim priority to U.S. Provisional Application No. 60/178,561 filed January 26, 2001. No new matter is added by virtue of these amendments. Accordingly, entry thereof is kindly solicited.

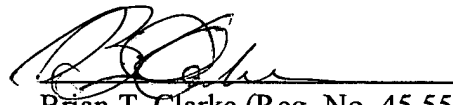
Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825.

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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Dated: May 24, 2001


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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Paragraph beginning at page 13, line 3, has been amended as follows:

– The Rad51 antisense molecules hybridize under normal intracellular conditions to the target nucleic acid to inhibit Rad51 expression or translation. In an alternative embodiment an anti-gene may be used. The target nucleic acid is either DNA or RNA. In one embodiment, the antisense molecules bind to regulatory sequences for Rad51. Alternatively, the antisense molecules bind to 5' or 3' untranslated regions directly adjacent to the coding region of the Rad51 gene. Preferably, the antisense molecules bind to the nucleic acid within 1000 nucleotides of the coding region, either upstream from the start or downstream from the stop codon. In a preferred embodiment, the antisense molecules bind within the coding region of the Rad51 gene. More preferably, the Rad51 antisense molecule is selected from the group consisting of AS4, AS5, AS6, AS7, AS8 and AS9 (SEQ ID NOS:4-9) as indicated in Figure 1 and Table 1 (SEQ ID NOS:1-9) below. Table 1 includes the recitation of “R51” before the same corresponding antisense, but “AS4” and “R51AS4”, for example, are used interchangeably herein. In one embodiment, the Rad51 antisense molecules are not directed to the structural gene; this embodiment is particularly preferred when the Rad51 antisense molecule is not combined with another antisense molecule. It is understood that any of the antisense molecules can be combined. –

Table 1, beginning at page 13, line 19, has been amended as follows:

– **Table 1: Antisense Oligonucleotide Sequences**

ANTISENSE IN CODING REGION	
R51AS1	5'- (P=S) GGC TTC ACT AAT TCC-3' (SEQ ID NO:1)
R51AS2	5'- (P=S) CGT ATG ACA GAT CTG-3' (SEQ ID NO:2)
R51AS3	5'- (P=S) GCC ACA CTG CTC TAA CCG 3' (SEQ ID NO:3)
ANTISENSE IN 5' UNTRANSLATED REGION	
R51AS4	5' (P=S) GGT CTC TGG CCG CTG CGC GCG G-3' (SEQ ID NO:4)
R51AS5	5' (P=S) GCG GGC GTG GCA CGC GCC CG-3' (SEQ ID NO:5)
ANTISENSE IN 3' UNTRANSLATED REGION	
R51AS6	5' (P=S) CCC AAG TCA TTC CTA AGG CAC C-3' (SEQ ID NO:6)
R51AS7	5' (P=S) GGG AGT ACA GGC GCA AGA CAC C-3' (SEQ ID NO:7)
R51AS8	5' (P=S) CGA TCC ACC TGC CTC GGC CTC CC-3' (SEQ ID NO:8)
R51AS9	5' (P=S) CCT CAG GCT ATA GAG TAG CTG GG-3' (SEQ ID NO:9)

Paragraph beginning at page 16, line 3, has been amended as follows:

– Additionally, and not by way of limitation, Rad51 inhibitor delivery may include the use of nuclear localization signal (NLS). This is especially preferred when the Rad51 inhibitor is a peptide. NLSs are generally short, positively charged (basic) domains that serve to direct the entire protein in which they occur to the cell's nucleus. Numerous NLS amino acid sequences have been reported including single basic NLSs, such as the SV40 (monkey virus) large T Antigen (Pro Lys Lys Lys Arg Lys Val (SEQ ID NO:10)) (Kalderon (1984), *et al.*, *Cell* 39:499-509), the human retinoic acid receptor- β nuclear localization signal (ARRRRP (SEQ ID NO:11)), NF κ B p50 (EEVQRKRQKL (SEQ ID NO:12)) (Ghosh *et al.*, *Cell* 62:1019 (1990)), NF κ B p65 (EEKRKRTYE (SEQ ID NO:13)) (Nolan *et al.*, *Cell*

64:961 (1991)), and others (see for example Boulikas, *J. Cell. Biochem.* 55(1):32-58 (1994)). All of these references are incorporated herein in their entirety by reference. Double basic NLSs are exemplified by that of the Xenopus (African clawed toad) protein, nucleoplasmin (Ala Val Lys Arg Pro Ala Ala Thr Lys Lys Ala Gly Gln Ala Lys Lys Lys Lys Leu Asp (SEQ ID NO:14)) (Dingwall, *et al.*, *Cell* 30:449-458, (1982); Dingwall, *et al.*, *J. Cell Biol.*, 107:641-849; (1988)). Numerous localization studies have demonstrated that NLSs incorporated in synthetic peptides or grafted onto reporter proteins or other molecules not normally targeted to the cell nucleus cause these molecules to be concentrated in the nucleus. See, e.g., Dingwall and Laskey, *Ann. Rev. Cell Biol.* 2:367-390, (1986); Bonnerot, *et al.*, *Proc. Natl. Acad. Sci. USA* 84:6795-6799, (1987); Galileo, *et al.*, *Proc. Natl. Acad. Sci. USA* 87:458-462, (1990). –

On page 22, immediately preceding the claims, the enclosed text entitled "SEQUENCE LISTING" was inserted into the text.

IN THE CLAIMS:

Claim 9 has been amended as follows:

- 9. The method according to Claim 4, wherein said Rad51 antisense molecule is selected from the group consisting of AS4, AS5, AS6, AS7, AS8 and AS9 (SEQ ID NOS:4-9). –